REMARKS

The present Request for Continued Examination (RCE) is responsive to the Advisory Action dated August 28, 2008, which in turn responds to many of the comments made by the Applicant in the Amendment after Final Action filed on August 8, 2008, but was not entered in the above-identified application. Specifically, the Applicant requests entry of the Amendment submitted herewith, as well as the Declarations of Mr. Yasuhiro Shindo and Dr. Takahiro Ito filed under the provisions of 37 CFR 1.132.

Claims 1-19 are cancelled, and new claims 20-34 substituted therefor.

Novelty of the Present Invention

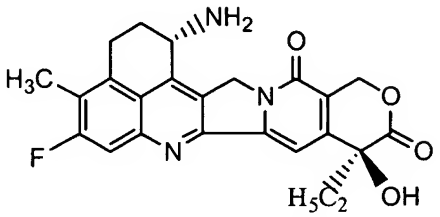
The term "consisting essentially of" is now recited in all of the claims. This amendment should obviate the anticipation rejection of the claims under 35 USC 102(b) over Harada et al. Therefore, this rejection is traversed and reconsideration thereof is requested.

Unobviousness of the Present Invention

Claims 1, 9 and 14-19 were previously rejected under 35 USC 103(a) as being unpatentable over Harada in view of Wall et al. This rejection is also respectfully traversed, and reconsideration thereof is requested.

In WO 02/05855 ("Reference 1"), which was published prior to the convention priority date of the present application, there are described DDS-camptothecin which is prepared by binding a camptothecin analog (Compound A) as shown below and a carboxy-bearing polysaccharide via gly-gly-phe-glycine, and a composition containing DDS-camptothecin.

Compound A:



Chemical name: (1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9- hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b] quinoline-10,13(9H,15H)-dione

In the case that said DDS-camptothecin is compared with the camptothecin analog in Wall et al., the DDS-camptothecin more closely resembles the camptothecin derivative directed to the present invention in respect of containing a carboxy-bearing polysaccharide as a constituent-component.

It is notably described in Reference 1 that since the preservative stability of a DDS-camptothecin preparation is extremely low, a sugar or a sugar alcohol (an excipient) should be mixed therewith in order to secure the preservative stability.

On the other hand, despite the fact that the preparation of the present invention contains a DDS-camptothecin derivative like the preparation described in Reference 1, the preparation of the present invention has a characteristic property to secure highly preservative stability by adjusting the pH to 5 to 8 with a buffer without mixing a sugar or a sugar alcohol as an ingredient. The fact that the present preparation has such a characteristic property is not obvious from Reference 1 as well as the Harada et al. and Wall et al. documents cited by the Examiner.

The ITO Declaration

In order to clarify the unobviousness of the preparation containing a DDS-camptothecin derivative of the present invention, a comparative experiment on long term preservative stability has been carried out between an aqueous preparation not containing an excipient, a sugar alcohol

(sorbitol), and an aqueous preparation containing an excipient, a sugar alcohol (sorbitol). The experiment and results are shown in a Declaration under 37 CFR 1.132 by Dr. Takahiro ITO, who is an inventor of the present invention.

As is clear from the results shown in the ITO Declaration, when the preparations are preserved at room temperature (25°C), the term (estimated term) which is taken for the residual rate of the drug to become 90% was 2.53 years with formulation 1, and 3.42 years with formulation 2. Concerning the stability of the drug, this result is unexpected. Thus, the former clearly has a practical value in comparison with the latter.

As such, it cannot be deduced from Harada et al. in view of Wall et al. that a skilled person in the art could obtain a preparation which has an extremely high preservative stability for a long term without adding a sugar or a sugar alcohol to the DDS-camptothecin compound.

Furthermore, it is clear from the description, such as the examples shown in the present specification, that a lyophilized preparation of the present invention also has an excellent preservative stability.

Thus, it is believed that claims 20-34, directed to a liquid preparation (claims 20-28, 30 and 32-34) and a lyophilized drug composition (claims 29 and 31), are novel and nonobvious over the prior art.

The SHINDO Declaration

In order to complete the record in this file and to provide additional evidence of the patentability of the presently claimed invention, the applicant hereby submits a Declaration under 37 CFR 1.132 executed by Mr. Yasuhiro Shindo. Entry of this document into the file is hereby requested. The Declaration contains an Attachment (two pages) which comprises data on T-0128 solutions as described in the Harada reference.

Table of Paragraph 1.1 of the Attachment

This Table shows the composition of the T-0218 solution disclosed in Paragraph 2.4 (lines 1-11) of the Harada et al reference (prior art). The prior art solution (pH 4) contains a conjugate (T-0218) at a concentration of 100 μg/mL corresponding to 10 mg/100 mL, namely 0.01 w/v% of T-0128. Therefore, the solution of the present invention is distinct from the prior art solution in terms of T-0128 content and pH.

Table of Paragraphs 1.2.1 to 1.2.3 of the Attachment

Each of the Tables shows the composition of the T-0128 solution disclosed in Paragraph 2.4 (line 11 to the end of the paragraph) of the prior art. Each of the prior art solutions buffered with acetate or phosphate at pH 3, 4, 5, 6 or 7 contains T-0128 at a concentration of 100 μg/mL, namely 0.01 w/v% of T-0128. Therefore, the solution of the present invention is distinct from the above prior art solution in terms of at least one of T-0128 content and pH.

Table of Paragraph 2 of the Attachment

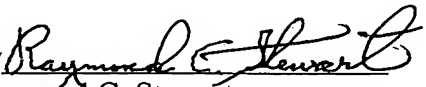
This Table shows the composition of the T-0128 solution for intravenous injection disclosed in Paragraph 2.5 of the prior art. According to this disclosure (line 4), T-0218 was dissolved in saline at 0.5 mg/mL of T-2513 corresponding to 10 mg/mL of T-0128 (namely, 1 w/v% of T-0128). However, it is clear that the prior art solution does not contain any buffer. Therefore, the solution of the present invention buffered at pH 5 to 8 is clearly distinct from the prior art solution.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Raymond C. Stewart Reg. No. 21,066 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.147; particularly, extension of time fees.

Dated: December 5, 2008

Respectfully submitted,

By 

Raymond C. Stewart
Registration No.: 21,066
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant

Attachments: Two Rule 132 Declarations